

Appl. No. : 10/523,863
Filed : January 17, 2006

REMARKS

Claim 2 has been amended to correct a spelling error and Markush language. Claim 12 has been canceled. New claims 13 and 14 have been added. Thus, claims 1-11, 13 and 14 are presented for examination. Support for the new claims may be found in the original claims and throughout the specification. No new matter has been added. Reconsideration and withdrawal of the present rejections in view of the following comments are respectfully requested.

Rejection under 35 U.S.C. §112, second paragraph

Claim 12 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite for reciting a use without any active, positive steps delimiting how this use is actually practiced. Although applicants do not agree with the rejection, claim 12 has been canceled herein solely to expedite prosecution of the application.

In view of the claim amendment, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Rejection under 35 U.S.C. §101

Claim 12 was rejected under 35 U.S.C. §101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper process claim. Although applicants do not agree with the rejection, claim 12 has been canceled herein solely to expedite prosecution of the application.

In view of the claim amendment, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §101.

Rejection under 35 U.S.C. 103(a)

Claims 1-11 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kass et al. (*J. Am. Chem. Soc.* 61:3292-3294, 1939) in view of Takagi et al. (*Lipids* 16:546-551, 1981).

Kass et al. teach the preparation of 10, 12, 14-octadecatrienoic acid (pseudo-eleostearic acid) by treating linseed oil fatty acids with potassium hydroxide in ethylene glycol, followed by crystallization. As acknowledged by the Examiner, Kass et al. does not teach: (1) purification of the resulting product by urea complexation or liquid chromatography; (2) the claimed linoleic acids, which differ from the linolenic acids of Kass et al. by positions of the double bonds (positional isomers); or (3) performing the method at about 20°C to about 280°C over a period of time from about 30 seconds to about 18 hours. The Examiner states that since “the extraction process for one isomer (is) reasonably applicable to the other isomer of the same compound”, that it would be obvious to apply the purification methods taught by Takagi et al. to prepare linolenic acids of Kass et al. in order to make the reaction product more effective and to achieve good yields, with a reasonable expectation of success. With regard to claim 10, the Examiner alleges that it would be obvious to use the method of claim 1 to obtain the compound recited in claim 10. However, as explained below, this combination of references would not render the claimed invention obvious.

Establishing *prima facie* obviousness requires a showing that some combination of objective teachings in the art and/or knowledge available to one of skill in the art would have lead that individual to arrive at the claimed invention. See *In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). Moreover, establishing *prima facie* obviousness requires not only a showing that such a combination of prior art teachings is possible, but also that the teachings would have motivated the skilled artisan to make the combination to arrive at the claimed invention. See *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir.1988). Absent a showing of such motivation, *prima facie* obviousness is not established. See *Fine*, 5 USPQ2d at 1598. The USPTO has acknowledged that the recent decision by the Supreme Court in *KSR Int’l. Co v. Teleflex Inc.*, No. 04-1350 (April 30, 2007) did not eliminate this requirement. In a Memorandum dated May 3, 2007 sent to Technology Center Directors, Margaret A. Focarino, Deputy Commissioner for Patent Operations, concluded that “in formulating a rejection under 35 U.S.C. § 103(a) based upon a combination of prior elements, it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed.” In the case of the present rejection, no such reason is present.

Kass et al. describe fully conjugated acid compounds that result from rather harsh reaction conditions, involving long reaction times in butanol, a high ratio of KOH/fatty acid and high temperature. Kass et al.'s method ends with a standard crystallization step in which the reaction mixture is diluted into a solvent and subjected to different temperatures in order to allow crystals to precipitate. This step is used twice: first, to remove saturated fatty acids from the fatty acids mixture obtained after linseed oil hydrolysis (double crystallization in ligroin at -18°C); and second, to isolate and purify pseudo-eleostearic acid overnight at -18°C in ligroin. Although Takagi et al. teach liquid chromatography for analysis of conjugated octadecatrienoic acids, there is no reason why one of ordinary skill in the art would substitute a liquid chromatography method for the crystallization method of Kass et al. Crystallization is performed twice in Kass et al., and there is no teaching that suggests modifying Kass et al. to instead use liquid chromatography to arrive at the invention defined in claim 1.

Crystallization is a chemical solid-liquid separation technique, in which mass transfer of a solute from the liquid solution to a pure solid crystalline phase occurs. Crystallization operates by a *nucleation* step and a *crystal growth* step. For nucleation to occur, the molecules must gather together on a nanometer scale and then become stable under certain operating conditions. These operation conditions include temperature, pressure and saturation levels. Nucleation often occurs relatively slowly as the initial molecules must collide into each other in the correct orientation and placement for them to adhere and form the crystal nuclei. Once the nuclei is formed, crystal growth may occur.

Liquid chromatography is a completely different process which does not involve a solid phase. This method involves passing a mixture dissolved in a liquid "mobile phase" through a liquid "stationary phase", which separates the "analyte" to be measured and separated from other compounds in the mixture. This separation technique is based on the polarity of the mobile and stationary phases.

There is insufficient basis to establish a *prima facie* case of obviousness with regard to Kass et al. in view of Takagi et al. The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 USPQ 1783 (Fed. Cir. 1992). Kass et al. teach that the 10,12,14 isomer is susceptible to crystallization but does not suggest the desirability of modifying the process to use another separation technique, much less liquid

chromatography. Takagi et al. teach that the 9,11,13 isomer can be subjected to liquid chromatography, but does not suggest the desirability of using such a process instead of a crystallization process.

As acknowledged by the Examiner, Kass et al. describe fully conjugated 10,12,14-octadecatrienoic acid, whereas Takagi et al. describe fully conjugated 9-11-13-octadecatrienoic acid. The Examiner notes that these linolenic acids are isomers. The Examiner contends that "*the extraction process for one isomer [is] reasonably applicable to the other isomer of the same compound.*", but provides no evidence in support of this statement.

MPEP 2144.09 states that "*Homology and isomerism involve close structural similarity which must be considered with all other relevant facts in determining the issue of obviousness.*" Homology should not be automatically equated with *prima facie* obviousness because the claimed invention and the prior art must each be viewed "as a whole." *In re Langer*, 465 F.2d 896, 175 USPQ 169 (CCPA 1972). Thus, neither homology nor isomerism should be equated with *prima facie* obviousness. The conjugation of an isomer is related to its stability and orientation, and stability and orientation of a compound determine what kind of synthesis and separation processes are desirable. There is no teaching that it would be desirable to modify the crystallization of one isomer with liquid chromatography separation of a different isomer, to arrive at the claimed invention which relates to isomers not described by either of these references.

Although these isomers have the same empirical formula and molecular weight, they are certainly not the same "compound". It is well known that chemical isomers often have unpredictably different properties in terms of chemical and biological reactivity, activity and stability which can lead to differences in susceptibility to and facility of separation. In fact, one isomer of a compound may be biologically active, whereas another isomer may be inactive. One or more of these properties may vary with the position of the double bonds. A fatty acid molecule comprises a carbon chain that will orient itself in relation to the carboxylic acid functional group depending on the carbon chain length and the location, orientation and degree of conjugation. The orientation of the carbon chain is an important factor in the reactivity and stability of fatty acids.

Thus, the cited references do not support the Examiner's position that all extraction processes are interchangeable for separation of positional isomers of fatty acids. Indeed, there is

a significant level of unpredictability in the art of separating conjugated fatty acids and isomers. Such that undue experimentation would have been necessary to arrive at the method of claim 1 based on the teachings of the prior art.

In view of the comments provided above, claim 1 cannot be *prima facie* over the cited references. In addition, claims 2-10, which depend on claim 1, are necessarily nonobvious over the cited prior art.

With regard to claim 10, the Examiner alleges that it would be obvious to apply the same method to prepare other isomers of octadecatrienoic acids and it would therefore be obvious to obtain 6Z, 8E, 12Z-octadecatrienoic acid using the method of claim 1. Because claim 1 is not obvious in view of the cited reference, then claim 10 is necessarily nonobvious..

In addition, neither of the cited references describes a 6Z,8E,12Z-octadecatrienoic acid, but rather describe other fatty acids which are tri-conjugated. Thus, these references do not disclose or suggest the claimed isomer. The Examiner generally cites MPEP 2144 which states that "*If such a species or subgenus is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on a reasonable expectation that structurally similar species usually have similar properties.*" As discussed above, there is not a reasonable expectation that such structural "similarities" would lead to sufficiently similar properties. Again, conjugated fatty acid isomers may have rather disparate properties in terms of chemical and biological reactivity. Depending on the degree and location of conjugation, the acid may be for instance anti-carcinogenic or not, and may be difficult or easy to synthesize or purify. The fatty acid of claim 10 is structurally distinct from the fatty acids of the prior art and one of ordinary skill in the art cannot reasonably predict whether it would have similar properties. The present inventors discovered that the method of claim 1, was unexpectedly able to isolate this octadecatrienoic acid. The Applicant was able to synthesize the acid defined in claim 10, which was purified after the reaction as shown in Table 6 of the specification.

Claim 11 is directed to a method for preparing 9Z,11E,15Z-octadecatrienoic acid and 9Z,13E,15Z-octadecatrienoic acid comprising (a) blending linseed oil with a base to produce a reaction mixture and (b) recovering said 9Z,11E,15Z-octadecatrienoic acid and 9Z,13E,15Z-octadecatrienoic acids from the reaction mixture.

Although this claim was included in the obviousness rejection, the Examiner did not comment on this claim in the rejection. Thus, Applicants assume that the Examiner did not intend to reject Claim 11 as obvious over these references. However, if this was the Examiner's intent, then Applicants reiterate their previous remarks regarding the disparate properties in terms of chemical and biological reactivity of positional isomers. The isomer recited in claim 11 is neither taught nor suggested by either of the cited references, would not reasonably be expected to have the same properties as the isomers disclosed in these references, and would not reasonably be expected to be amenable to the separation techniques disclosed in these references.

In view of the comments presented above, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a).

Obviousness-type double patenting rejection

Claim 11 was provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of copending U.S. Application No. 10/567,419.

The Examiner states that claim 11 and the claims of the copending application "generally overlap", and that the difference between claim 11 and the claims of the copending application relates to "*the ratios of the components in the mixture, whereas the instant application is silent as to these ratios*".

Claim 1 of the copending application includes the step of blending one or more vegetable oils "in the presence of water", whereas claim 11 does not include this step. Claim 11 includes the step of blending linseed oil with a "base" to produce the reaction mixture.

In view of the comments provided above, Applicants respectfully request reconsideration and withdrawal of the obviousness-type double patenting rejection.

Appl. No. : 10/523,863
Filed : January 17, 2006

Comments regarding new claims

New claim 13 recites a method of preparing conjugated linolenic acids comprising the steps of (a) blending vegetable oils and/or fats including linolenic acids with a base to produce a reaction mixture, (b) recovering said conjugated linolenic acids from the reaction mixture, and (c) subjecting the reaction mixture to urea complexation. Urea complexation is neither disclosed nor suggested by the cited references, and enables up to and over 40% enrichment, as stated at page 10 of the published PCT application (PCT WO2004/013078). New claim 14 further recites this method as having a subsequent step of liquid chromatography. The product is obtained in over 90% purity by simple preparative chromatography, as stated at page 10 of the published PCT application (PCT WO2004/013078). Thus, new claims 13 and 14 are also not obvious in view of the cited references.

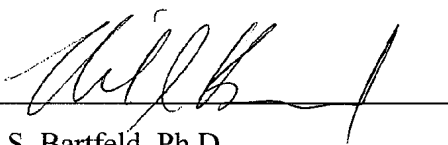
CONCLUSION

In view of the foregoing amendments and comments, it is respectfully submitted that the present application is fully in condition for allowance, and such action is earnestly solicited. If any minor issues remain which could be resolved by telephone, the Examiner is invited to contact the undersigned at the number provided below.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: July 23, 2007

By: 
Neil S. Bartfeld, Ph.D.
Registration No. 39,901
Agent of Record
Customer No. 20,995
(619) 235-8550

4045098
072307